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10/673,575	09/30/2003	Sudhir K. Sinha	P56885	2640

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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,575	SINHA ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. BABIC	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,21,22 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *27 and 30* is/are allowed.

6)☒ Claim(s) *1,7,8,21,22,26 and 29* is/are rejected.

7)☒ Claim(s) *5,6,25, and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claim(s) 1, 5-9, 21, 22, and 25-30 are pending. The following Office Action is in response to Applicant's communication dated July 7, 2008.

Claim Rejections - 35 USC § 103 - Withdrawn

Applicant remarks regarding the rejection of claim 5 over Sifis, Palmirotta, Jurka, and Buck (see pg. 12) are sufficient to overcome the grounds of the rejection. Applicant shows unexpected results of the intra-Yb8 method. Thus, the rejection has been withdrawn. Subsequently, the rejections of claims 25 and 28 have been withdrawn as well.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim(s) 1, 7, 8, 21, 22, 26, and 29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6), and in further view of Fortina et al. ("Non-radioactive detection of the most common mutations in the cystic fibrosis transmembrane conductance regulator gene by multiplex allele-specific polymerase chain reaction" Hum Genet. 1992 Dec;90(4):375-8).

With regard to claim(s) 1, 21, and 22, Sifis teaches a method (pg. 589, 590, materials and methods, for example) comprising: providing a sample to be analyzed (pg. 589, 590, materials and methods, amplification, for example); amplifying predetermined genomic DNA containing an Alu element by using primers (pg. 589, 590, materials and methods, amplification, for example), the amplification being intra-Alu

polymerase chain reaction amplification (pg. 589, 590, materials and methods, amplification, for example); and measuring the amount the human DNA by comparing the amplified DNA with a reference (fig. 1, 2; pg. 589, 590, materials and methods, amplification, for example).

With regard to claim 8, Sifis teaches detecting the human DNA using a quantitative PCR system (pg. 590, col. 1, for example).

Sifis further teaches that the assay is based on the amplification of core Alu sequences, i.e. intra-Alu PCR, from primate DNA (pg. 589, 590, materials and methods, amplification, for example). Sifis further highlights that it is desirable that any method of quantitation be primate specific; otherwise, any substantial contamination may lead to overestimation of the amount of primate DNA within the sample DNA extract.

Such a disclosure agrees with findings of Palmirotta, which teaches the PCR amplification of Alu sequences for the specific purpose of determining the origin of the DNA (i.e. human DNA or non-human primate DNA) (pg. 432, col. 1, PCR amplification, for example). Palmirotta expressly teaches that PCR-based methods targeting human Alu sequences may contribute to the evaluation of biological samples of suspected human origin (pg. 431, col. 2, para. 4, for example). Thus, it is clear from the teachings of Palmirotta that the amplification of Alu sequences that are not exclusively contained within the human genome, from an unknown nucleic acid sample, can lead to amplification of unwanted primate DNA, e.g. non-human primates DNA.

With regard to claim 7, Palmirotta teaches detecting the human DNA on an agarose gel stained with ethidium bromide (Figure 1).

None of the above references however, expressly teach the amplification of Alu sequences that are contained exclusively in the human genome through the use of mutation specific primers.

Batzer provides a supporting disclosure that teaches the discovery of mutation specific Alu sequences exclusively contained within the human genome, such as the Ya5 subfampliy (fig. 1, for example). Batzer further teaches that the younger subfamilies are considered a "gold standard" within the art (pg. 4, for example). It is clear from the teachings of Batzer that Alu sequences exclusively contained within the human genome were well known in the art at the time of invention. Batzer does not expressly teach the amplification of human Alu sequence with mutation specific primers.

Fortina provides a supporting disclosure that teaches the detection of a common mutation within a target sequence utilizing primers that target the mutation (abstract; pg. 354, materials and methods, primer targeting ΔF508, for example). Fortina clearly shows that primers targeting a particular mutation aid in detecting the presence of such a mutation by allowing amplification of the target sequence.

Thus, in summary, it is submitted that it would have been prima facie *obvious* to a skilled artisan at the time of invention, wanting to quantify human DNA from an unknown source through the method of Sifis, to target and amplify an Alu known to reside strictly within the human genome, such as Ya5, in order to obtain accurate human results.

Furthermore, it would have been *prima facie* obvious to a skilled artisan at the time of invention, wanting to target a specific Alu specific mutation, to design primers to

target subfamily-specific mutations within human Alu sequences such that particular subfamily human Alu sequences are amplified since the prior art demonstrates such primers useful in such a capacity.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

With respect to Applicant's arguments regarding expectation of success, such a standard does not require an expectation of achieving results similar, the same, or even better than that of the prior art.

Furthermore, a consensus within the prior art indicating that a task might be difficult, e.g. designing mutation specific primers to amplify a sequence of high GC content, does not necessarily mean a skilled artisan would have found such a task unachievable in a reasonably predictable manner. First, the mere fact that Sifis teaches the amplification of core Alu sequences provides evidence that a skilled artisan would have found the development of primers to amplify such regions reasonable achievable. The same reasoning applies to that of mutation specific primers and Fortina. Moreover, the fact that Applicant references using software packages to develop their primers (see remarks pg. 12) only adds to the expectation of success that a skilled artisan would have recognized at the time of invention. Such computer programs were designed specifically to make the selection of suitable primers easier and less time consuming by employing algorithms to produce the primers having the characteristics most likely to allow amplification of a target region.

With respect to Applicant's arguments regarding the lack of a teaching, suggestion, or motivation to combine the cited references, the examiner has provided a reasoning to combine the prior art. MPEP 2144 recites, "The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). >See also Dystar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick, 464 F.3d 1356, 1368, 80 USPQ2d 1641, 1651 (Fed. Cir. 2006).* In the instant case, the prior art establishes that the amplification of an Alu sequence known to reside in various primates may lead to inaccurate quantitative results of the desired sequence from the desired primate (e.g. humans). Furthermore, Alu sequences existing only in humans were known at the time of invention. Thus, a skilled artisan wanting to quantify human DNA from a sample possibly containing DNA from multiple different primates would have been motivated to target and amplify Alu sequences existing only in humans through techniques known at the time of invention, e.g. allele-specific amplification.

With respect to Applicant's arguments regarding Fortina teaching away from the claimed invention, the claimed invention does not require that a 5' and 3' primer be allele specific. Thus, such arguments are commensurate in scope with the claimed invention. However, even such a limitation was introduced; Fortina clearly provides the

reasoning/motivation to make such a modification, as the modification would simply add to the specificity of the amplification product.

Thus, the rejection is maintained.

2. Claim(s) 9 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6), and in further view of Fortina et al. ("Non-radioactive detection of the most common mutations in the cystic fibrosis transmembrane conductance regulator gene by multiplex allele-specific polymerase chain reaction" Hum Genet. 1992 Dec;90(4):375-8) as applied to claim 1 above, and in further view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-erbB-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

The methods of the previously applied references have been outlined in the above rejections. The previously applied references do not specifically disclose the practice of a quantitative PCR system such as TaqMan.

Gelmini provides a supporting disclosure that teaches the practice of a quantitative PCR system using TaqMan chemistry (fig. 1,2,3; table 1; pg. 754, Columns 1,2, for example). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (pg. 752, col. 2, para. 2, for example).

Thus, in summary, it is submitted that it would have been *prima facie* obvious to a skilled artisan at the time of invention to incorporate a quantitative PCR system into the methods of Sifis since Gelmini suggests such a modification for among other reasons, to circumvent post-PCR product quantitation procedures.

Response to Arguments

Applicant's arguments have been addressed in the response(s) set forth above.

Allowable Subject Matter

Claims 5, 6, 25, and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 27 and 30 are allowable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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